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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,128	08/29/2005	Bronislava Gedulin	54061.8101.US00	7370

44638 7590 09/05/2007

Intellectual Property Department
Amylin Pharmaceuticals, Inc.
9360 Towne Centre Drive
San Diego, CA 92121

EXAMINER	
LI, RUIXIANG	

ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
09/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,128	GEDULIN ET AL.	
	Examiner	Art Unit	
	Ruixiang Li	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-3,5-12 and 14-21* is/are pending in the application.

4a) Of the above claim(s) *7 and 15-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,6,8-12 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 04/20/2007 has been entered.

Claims 1-3, 5-12, and 14-21 are pending. Claims 1-3, 5, 6, 8-12, and 14 are under consideration.

Withdrawn Objections and/or Rejections

The rejection of claims 1-3, 5, 10, and 13 under 35 U.S.C. 102(a) as being anticipated by El-Salhy et al. (Peptides 23:397-402, February 2002) is withdrawn in view of Applicants' argument.

Claim Rejections Under 35 U.S.C.§112, 1st Paragraph (Written Description)

(i). The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(ii). Claims 1-3, 5, 6, and 8-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Claims 1-3, 5, 6, and 8-12 are drawn to a method of treating an intestinal damage comprising administering a pharmaceutically active formulation of PYY or a PYY agonist to a subject to treat the intestinal damage, wherein said PYY or said PYY agonist is a peptide that comprises an active fragment of PYY. The specification defines PYY as a peptide YY polypeptide obtained or derived from any species, and defines PYY agonist as any compound which elicits an effect of PYY to protect from or reduce colon injury associated with inflammatory bowel disease or ulcerative colities and which binds specifically in a Y receptor assay or in a competitive binding assay (page 10). Thus, the claims are drawn to a method comprising administration of PYY or a genus of structurally undefined PYY agonists because the limitation recited in the claims says nothing about the characteristic structure of the PYY agonists.

The specification fails to provide any critical structural feature to adequately describe the genus of PYY agonists that may be administered in the claimed method. The specification merely discloses two compounds, a human PYY of SEQ ID NO: 2 and PYY (3-36) of SEQ ID NO: 3, which are not sufficiently representative of the genus of PYY agonists. There is no disclosure of a defined relation between function and structure of the PYY agonists. There is even no identification of any particular portion of the structure that must be conserved. While the claim requires that PYY agonist comprise an active fragment of PYY, it does not say what the active fragment is. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the genus of PYY agonists.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of the PYY agonists, and therefore conception is not achieved until reduction to practice has occurred. Therefore, only the method of administering PYY and PYY (3-

36), but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph.

(iii). Response to Applicants' argument

Applicants review the legal standard for written description and argue that the instant claims are not drawn to a genus of compounds per se, but rather to novel uses of those compounds. Applicants argue that as amply disclosed throughout the instant application, administration of PYY or agonists thereof has an effect, for example to reduce intestinal damage and to restore bowel mucosa or bowel function. Applicants argue that the instant application and references incorporated therein in their entirety disclose numerous exemplary PYY and PYY agonists that comprises an active fragment of PYY, as recited in the instant claims, that may be selected by in order to practice the instantly claimed methods, e.g., useful as agents to reduce intestinal damage, such as bowel atrophy, and to restore bowel mucosa or bowel function.

Applicants' argument has been fully considered, but is not deemed to be persuasive for the following reasons. First, the requirement for written description under 35 U.S.C. 112, first paragraph is applicable to a method of using a genus of compounds. A genus of compounds to be used in a method needs to be adequately described. If a genus of compounds does not meet the requirement for written description, a method of using such a genus of compound does not meet the requirement for written description.

Secondly, the specification merely discloses two compounds, a human PYY of SEQ ID NO: 2 and PYY (3-36) of SEQ ID NO: 3, which are not sufficiently representative of the genus of PYY agonists because the claims are drawn to a method comprising administration of PYY or a genus of structurally undefined PYY agonists. The claims recite a limitation "wherein said PYY or said PYY agonist is a peptide that comprises an active fragment of PYY". However, the specification does not disclose the structure of the active fragment of PYY; nor does the claims indicate what the active fragment of PYY is. Moreover, the prior art does not provide compensatory structural or correlative teachings to enable one skilled in the art to identify the encompassed genus of PYY agonists.

Finally, methods of identifying PYY agonists as disclosed at pages 24-28 of the specification are not equivalent to the methods of making a PYY agonist in the context of treating intestinal damage because they do not provide the information on the conserved structure critical to the PYY activity.

Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the genus of PYY agonists and thus methods of using the genus of PYY agonists.

Claim Rejections Under 35 U.S.C.§102 (b)

(i). The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(ii). Claims 1, 2, 5, and 10-12, are rejected under 35 U.S.C. 102(b) as being anticipated by Balasubramaniam (U. S. Patent No. 5,604,203, Feb. 18, 1997).

Balasubramaniam teaches PYY and functional analogs and pharmaceutical formulations comprising PYY or an analog of PYY (column 15). Balasubramaniam also teaches treating gastrointestinal disorders, especially infectious or inflammatory diarrhea, or diarrhea resulting from surgery (column 16). Inflammatory diarrhea includes Crohn's disease (column 7), a form of inflammatory bowel disease, with PYY and its analogues (column 7). Balasubramaniam teaches that the compounds can be administered orally or parenterally (intravenously or subcutaneously) (column 14). The daily dose in the case of oral administration is typically in the range of 0.1 to 100 mg/kg body weight, and the daily dose in the case of parenteral administration is typically in the range of 0.001 to 50 mg/kg body weight (column 16). Thus, the teachings of Balasubramaniam meet the limitations of claims 1, 2, 5, and 10-12.

Response to Applicants' argument

Applicants argue that Balasubramaniam does not teach or fairly suggest a method of treating intestinal damage, comprising administering a PYY or PYY agonist polypeptide

in order to treat the intestinal damage, as instantly claimed. Applicants argue that the reference fails to provide any nexus between the alleged effects of administration of the disclosed compounds on water and nutrient absorption, cell proliferation, and blood flow regulation and methods of treating intestinal damage comprising administering PYY or a PYY analog polypeptide, as instantly claimed. Applicants argue that the reference is absolutely silent with regard to a method of treating intestinal damage per se, and is similarly silent with regard to a method of treating intestinal damage that may be associated with the disorders disclosed in the reference. Applicants argue that the reference fails to teach or suggest all of the elements of the instantly claimed methods.

Applicants' argument has been fully considered, but is not deemed to be persuasive because Balasubramaniam teaches treating gastrointestinal disorders, especially infectious or inflammatory diarrhea, or diarrhea resulting from surgery (column 16). Inflammatory diarrhea includes Crohn's disease (column 7), a form of inflammatory bowel disease, with PYY and its analogues (column 7). Thus, Balasubramaniam teaches administering PYY to a subject to treat intestinal damages associated with these diseases.

Claim Rejections Under 35 U.S.C.§103 (a)

(i). The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention

was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

(ii). Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Balasubramaniam (U. S. Patent No. 5,604,203, Feb. 18, 1997), as applied to claims 1, 2, 5, and 10-12 above, and further in view of Dumont et al. (Brain Res. Mol. Brain Res. 26: 320-324, 1994).

Balasubramaniam teaches a method of treating an intestinal damage comprising administering a pharmaceutically active formulation of PYY or a functional PYY analog to a human subject as applied to claims 1, 2, 5, and 10-12 above.

Balasubramaniam fails to teaches the method of claim 14, comprising administering PYY[3-36].

Dumont et al. teach a PYY agonist, PYY[3-36] that binds PYY receptors (see Abstract).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use PYY[3-36] in the method of treating a gastrointestinal disorder, such as Crohn's disease (a form of inflammatory bowel) as taught by Balasubramaniam with a reasonable expectation of success. One would have been motivated to do so because Balasubramaniam teaches PYY and PYY agonists can be used to treat a gastrointestinal disorder, such as Crohn's disease, whereas PYY [3-36],

which binds to PYY receptors, is expected to have the same effect in treating a gastrointestinal disorder, such as Crohn's disease.

Response to Applicants' argument

Applicants argue that Balasubramaniam fail to teach a method of treating intestinal damage comprising administering a pharmaceutically active of PYY or a PYY agonist polypeptide as instantly claimed for the reasons provided above. Applicants' argument has been fully considered, but is not deemed to be persuasive for the reasons set forth above.

(iii). Claims 1-3, 5, 10, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over El-Salhy et al. (Peptides 23:397-402, February 2002).

El-Salhy et al. teach a decreased level of PYY in human patients with gastrointestinal disorders, including inflammatory bowel diseases (examples are Crohn's colitis and ulcerative colities; pages 398-399). El-Salhy et al. also teach that the changes in PYY in gastrointestinal disorders could be beneficial in clinical practice and that in cases where PYY increase is desirable, diet that increases PYY synthesis and release can be followed, or a receptor agonist can be utilized (Abstract; page 401). El-Salhy et al. further teach that infusion of PYY in dogs increases colonic absorption of water, Na and Cl ions and PYY or its analogue can be of use as clinical agents in intestinal malabsorption disorders or after bowel resection (page 401).

El-Salhy et al. do not explicitly teach the instantly claimed method.

However, it would have been obvious to one having ordinary skill in the art at the time the invention was made to administer to a subject or a human patient after bowel resection or to treat a gastrointestinal disorders, including inflammatory bowel diseases (such as ulcerative colities) with a reasonable expectation of success. One would have been motivated to do so because of the teachings of El-Salhy et al. as stated immediately above.

Objection to claim 1

Claim 1 is objected to because it recites "wherein said PYY or said PYY agonist is a peptide that comprises an active fragment of PYY". Since PYY necessarily comprises an active fragment of PYY, the limitation "wherein said PYY is a peptide that comprises an active fragment of PYY" is not necessary. Appropriate correction is required.

Conclusion

No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00

pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

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PRIMARY EXAMINER

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August 31, 2007